

Application No. 10/647,156
Attorney Docket No. 01-1387
Response to Office Action dated September 11, 2008

REMARKS

Claims 45-52, 56-61, 63, 64, 66, 67 and 69 - 73 are pending. Claims 53-55, 62, 65 and 68 have been cancelled without prejudice or disclaimer in order to expedite the prosecution of the present application. Claims 45, 60 and 61 have been amended. No new subject matter has been added.

35 U.S.C. §112 Second Paragraph

The Examiner rejected claims 45-61, 63, 64, 66 and 67 under 35 U.S.C. 112 as being indefinite for failing to particularly point out and distinctly claim the invention.

- a. The Examiner objected to the use of the term “carboxamide compounds comprised of” and suggested adopting the language “A carboxamide compound of formula.” Applicant has amended the claims to incorporate the Examiner’s suggestion.
- b. The Examiner rejected claims 45 for use of the term “independent of one another”. Applicant has deleted this term.
- c. The Examiner rejected claim 45, 60, 61 and 66 for inconsistent use of the specific terms involving “salts”. While applicant does not agree with the Examiner’s position, solely for the purposes of advancing prosecution applicant has amended the claims to recite the term “pharmaceutically acceptable salts thereof” in order for the claims to be consistent.
- d-f. The Examiner rejected claims 53 -55 for lack of antecedent basis and inconsistency. Applicant has amended cancelled the claims thereby removing the basis for the rejection.
- g. The Examiner rejected claim 67 for reciting the “use” of a carboxamide compound without reciting a step or process. Applicant has deleted this claim thereby removing the basis for this rejection as well as the Examiner’s 35 U.S.C §101 rejection.

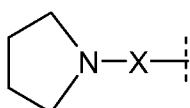
35 U.S.C. §112 Enablement

The Examiner rejected claims 45-59, 61, 63, 64, 66 and 67 under 35 U.S.C. §112 and has taken the position whereas the specification teaches making and using

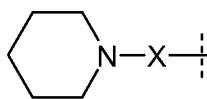
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compounds of formula I.1 wherein $-\text{NR}^1\text{R}^2$ is pyrrolidinyl, piperdinyl, morpholine or dialkylamino, but does not provide enablement for making and using compounds of formula I.1 wherein $-\text{NR}^1\text{R}^2$ is another moiety. Applicant respectfully disagrees with the Examiners conclusion that the rejected claims are not properly enabled. However, in the interest of advancing prosecution the applicant has narrowed the scope of the claims in light of the rejections. Applicant reserves the right to pursue amended subject matter in continuation and/or divisional applications. The amendments to the instant claims include:

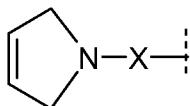
- In base claim 45 applicant has narrowed the definition of R^1R^2 to the genus of claimed heterocycles rings to those that are specifically exemplified. The claim does embrace a morpholino group which is not specifically exemplified but Examples 1.16 is a close analog and someone skilled in the art would know to make and use MCH antagonist compounds of formula I.1 having a morpholino group in this position.



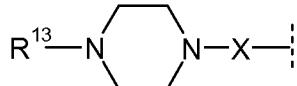
Ex. 2.1 etc.



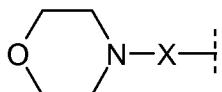
Ex. 2.3 etc.



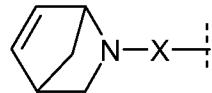
Ex. 2.103, 2.104,
2.121, 2.122



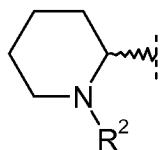
Ex. 2.80
analog 2.50, 2.51



analog 1.16, 4.6



Ex. 2.81



Ex. 2.105

- In the definition of R^1R^2 applicant has deleted the option that the ring connected to the heterocycle may be substituted with R^{20} .

Wands Factors - The Examiner provides discussion the Wands factors. Applicant submits the instant claims are properly enabled as discussed.

- 1) **Breath of the Claims** – The Examiner points to claims of NR^1R^2 which cover a list of moieties including substituted and non-substituted heterocycles. The heterocycles can be substituted with groups at R^{14} and R^{20} . Applicant submits that the instant claims are properly enabled. The compounds claimed in the instant claims according to formula I.1 are MCH R1 receptor antagonists. Compounds having substituents in the amine moiety also have antagonistic activities. It is within the ordinary skill of the art to synthesize compounds including the morpholino variation in the substituents within the scope of the instant claims given the close analogs that are provided.

- 2) **Amount of direction or guidance presented** - The Examiner asserts that the specification fails to adequately teach methods for making compounds of formula I.1 with rings added to the quinazoline ring throughout the full scope of the claims. The Examiner also states that the biological activity for the species made can not be extrapolated to other compounds of formula I.1 due to

the different structural attributes of the moieties claimed for NR^1R^2 . Applicant respectfully disagrees with the Examiner's position. The specification provides both general processes as well as specific examples of methods for making compounds according to the instant claims of formula I.1. Reaction schemes 1, 3, 4, 5, 7, 9, 10, 11, 13 disclose a general process for making compounds of formula I.1 and are not limited to any specific amine. Thus, reactions can be performed with amines as defined in claim 1. Reaction schemes 2, 6, 8, 12, 14 teach methods employing specific amines and these methods can be modified by one skilled in the art such that compounds with other amines according to the instant claims can be obtained. These modifications are within the ordinary skill of a chemist, including the knowledge as described in this application and its experimental part.

The Examiner takes the position that there are limited working examples to specific rings for $\text{-NR}^1\text{R}^2$ and that someone skilled in the art would not be able to extrapolate from the specification procedures with other moieties claimed for I.1. Contrary to the Examiner's position that there numerous working examples to specific rings for $\text{-NR}^1\text{R}^2$. For example,

<u>Group</u>	<u>Example</u>
- azetidinyl:	2.84, 2.102
- pyrrolidinyl:	2.1 etc.
- piperidinyl:	2.3 etc.
- dihydropyrrolyl:	2.103, 2.104, 2.121, 2.122
- piperazinyl:	2.80, 2.50, 2.51
- morpholinyl:	1.16, 4.6
- azabicycloheptenyl:	2.81
- piperidin-2-yl:	2.105

Although some of these examples (1.16, 2.50, 2.51, 4.6) are not covered by the restricted scope of the claim 45, the described methods also apply to the synthesis of the compounds according to the claim 45.

- 3) State of the prior art** - the Examiner states that there is no reference where a biphenyl -(phenyl-ethyl) amide is substituted with another group such as: azepine, spirocycle or with other substituents such as claimed. The Examiner also claims that there is no guidance to substantiate making and using compounds such as those claimed. This argument is no longer applies given the narrowed scope of the instant claims for the reasons described above.
- 4) Relative skill of those in the art** - The Examiner asserts that the skilled artisan would have to carry out extensive research to select compounds from the large Markush group of compounds represented by formula I.1. This argument no longer applies given the narrowed scope of the instant claims for the reasons described above.

5-6) Predictability or unpredictability of the art and quantity of experimentation required - The Examiner states that due to the pharmaceutical arts are unpredictable and that the specification has not provided sufficient support or guidance to show how to make the compounds of general formula I.1. The argument is no longer applies given the narrowed scope of the instant claims for the reasons described above.

Claim Objections

The Examiner rejected claim 60 as being improperly dependent in a rejected base claim. Applicant amended the base claim to remove this basis for rejection. Applicant has also deleted compounds 8 and 25 as pyridyl since this is not covered by the base claim.

Applicant also has become aware that the definition for R^{13} was inadvertently omitted in base claim 45. R^{13} is used in the piperazinyl-group of $R^1R^2N^-$.

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Originally R¹³ was defined as having the same meaning as R¹⁷. Support can be found in the specification in claim 1. Applicant has restricted the definition to R¹³ to H, alkyl and alkylcarbonyl.

Applicants thank the Examiner for the thorough review of the application. In view of the above amendments and remarks, Applicants respectfully submit that all objections and rejections have been addressed and respectfully request reconsideration of the instant application. If any points remain at issue which can best be resolved by way of a telephonic or personal interview, the Examiner is kindly requested to contact the undersigned at the telephone number listed below.

Respectfully submitted,

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